



NOTES TRISOMIES

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- **Genetic disorders:** trisomies (three copies of particular chromosome) → severe multi-organ defects (cardiac, gastrointestinal, genitourinary), debilitating dysmorphic features

CAUSES

- Meiotic nondisjunction (most common, > 90%)
- Mutation (e.g. translocation)
 - Mitotic nondisjunction → mosaicism

RISK FACTORS

- Advanced maternal age

COMPLICATIONS

- Widespread organ dysfunction

SIGNS & SYMPTOMS

- Depend on trisomy, affected organs

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound

- Prenatal diagnosis
 - Nuchal translucency, organ defects

LAB RESULTS

- Prenatal diagnosis
 - Chorionic villus sampling, amniocentesis
- Postnatal diagnosis
 - Karyotyping

OTHER DIAGNOSTICS

- Postnatal diagnosis
 - Clinical identification of dysmorphic features

TREATMENT

OTHER INTERVENTIONS

- Genetic counseling

DOWN SYNDROME

osms.it/down-syndrome

PATHOLOGY & CAUSES

- Autosomal trisomy of chromosome 21
- Most common chromosomal abnormality in live births, cause of intellectual disability

- Range of dysmorphic features, congenital anomalies (e.g. [congenital heart](#), otolaryngeal, gastrointestinal, hematologic, endocrine, urogenital defects)

CYTOGENETIC TYPES

- Meiotic nondisjunction in one parent (most common) → trisomy 21 (47 XY, +21)

VISIT...

LANZAROTE
Caliente.COM

- Chromosome 21 involved in [Robertsonian translocation](#)
- Trisomy 21 mosaicism due to mitotic nondisjunction
 - Some cells unchanged (46 XY), others (47 XY, +21)
 - Duodenal atresia/stenosis, tracheoesophageal fistula, cervical spine instability, hematologic disorders

RISK FACTORS

- [Advanced maternal age](#), previous child with trisomy 21, parental consanguinity

COMPLICATIONS

- Cardiac
 - Valve disease (e.g. mitral valve prolapse)
- Developmental delay, intellectual disability (IQ: 20–75)
- Endocrine
 - Hypothyroidism, obesity
- Gastrointestinal
 - Delayed dental eruption, [duodenal atresia](#), celiac disease
- Genitourinary
 - Cryptorchidism, infertility (in individuals who are biologically male)
- Hematologic
 - Anemia, ↑ risk of leukemia
- Musculoskeletal
 - Atlantoaxial instability (↑ mobility of C2 in relation to C1); juvenile idiopathic arthritis, hip dislocation
- Neurologic/psychiatric
 - [Early onset dementia](#) (by age 55), major depressive disorder, seizures
- Premature aging
- Respiratory
 - Tracheal stenosis, obstructive apnea
- Sensory
 - Congenital cataracts, hearing loss, frequent otitis media

SIGNS & SYMPTOMS

- [Brushfield spots](#) (small white/grayish spots on periphery of iris)

- Dysmorphic features
 - Microcephaly, flat occiput, [flattened face](#); [epicanthal folds](#); flat nasal bridge; upward-slanting palpebral fissures; small nose/mouth; protuberant tongue; low-set/small ears; short neck, excessive nuchal skin; shortened extremities; big [gap between first toe](#) (hallux), [others](#); [single transverse palmar crease](#); short fifth finger with clinodactyly
- Gastrointestinal
 - Vomiting, constipation, poor appetite, ↓ weight gain
- Neuromuscular
 - Hypotonia, diastasis recti (abnormally large inter-recti distance)
- Pale, dry skin; fatigue
- Respiratory
 - Dyspnea, wheezing



Figure 29.1 An eight-year-old boy with Down syndrome.

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound

- Prenatal diagnosis
 - Nuchal translucency (weeks 11–14)

LAB RESULTS

- Chorionic villus sampling/amniocentesis
- Prenatal diagnosis
 - ↓ pregnancy-associated plasma protein A (PAPP-A), unconjugated estriol (uE3), alpha-fetoprotein (AFP)
 - ↑ serum beta human chorionic gonadotropin (β -hCG), inhibin A
 - Quadruple screen
- Postnatal diagnosis
 - Fluorescence in situ hybridization (FISH), karyotyping

OTHER DIAGNOSTICS

- Postnatal diagnosis
 - Clinical identification of dysmorphic features



Figure 29.2 The feet of an individual with Down syndrome. There is a large space between the great and second toes.

TREATMENT

OTHER INTERVENTIONS

- Prenatal genetic counseling
- Supportive management of affected body systems

EDWARDS SYNDROME

osms.it/edwards-syndrome

PATHOLOGY & CAUSES

- Autosomal trisomy of chromosome 18
- Second most common autosomal trisomy in live births

CYTOGENETIC TYPES

- Meiotic nondisjunction in one parent (most common)
 - Trisomy 18 (47 XY, +18)
- Translocation of chromosome 18
- Trisomy 18 mosaicism due to mitotic nondisjunction
 - Some cells unchanged (46 XY), others (47 XY, +18)

RISK FACTORS

- Family history, more common in individuals who are biologically female (3:1), advanced maternal age

COMPLICATIONS

- ↑ risk of neoplasms (e.g. Wilms' tumor, hepatoblastoma)
- Multi-organ abnormalities (e.g. [cardiac septal defects](#), intestinal malrotation, Meckel's diverticulum, neurological disorders, horseshoe kidney, hypotonia, pulmonary hypoplasia, cryptorchidism)
- Failure to thrive (FTT)
- Severe developmental, cognitive impairment

- ↓ life expectancy (< one year old); up to 50% die within first week

SIGNS & SYMPTOMS

- Dyspnea, hypotonia, wheezing, lack of appetite, severe **mental disability**, poor weight gain
- Dysmorphic features
 - **Clenched hand/overlapping fingers**; microcephaly, **prominent occiput**; **small mouth**, **low-set** pointy **ears**; short sternum; ocular hypertelorism; abnormal retinal pigmentation; short nose with upturned nares; clubfeet, **rocker bottom feet**; scoliosis, narrow pelvis

DIAGNOSIS

DIAGNOSTIC IMAGING

Abdominal ultrasound

- Postnatal diagnosis
 - Presence of tumors

Ultrasound

- Prenatal diagnosis
 - Unchanged inhibin A; nuchal translucency (weeks 11–14)

LAB RESULTS

- Prenatal diagnosis
 - Amniocentesis/chorionic villus sampling (CVS), ↓ PAPP-A, serum β -hCG, uE3, AFP, quadruple screen
- Postnatal diagnosis
 - Fluorescence in situ hybridization (FISH), karyotyping

OTHER DIAGNOSTICS

- Prenatal
 - **Growth restriction**: umbilical cord with two vessels; persistent clenched/overlapping fingers; heart defects; cystic hygroma; polyhydramnios, oligohydramnios; intrauterine growth delay; omphalocele; hydrocephalus; agenesis of corpus callosum; Dandy–Walker abnormality; diaphragmatic hernia
- Postnatal
 - **Clinical identification**: dysmorphic features

TREATMENT

OTHER INTERVENTIONS

- Treat life-threatening/disabling conditions (e.g. infections, cardiac/gastrointestinal defects)
- Prenatal genetic counseling
- Psychosocial management

PATAU SYNDROME

osms.it/patau-syndrome

PATHOLOGY & CAUSES

- Autosomal trisomy of chromosome 13

CYTOGENETIC TYPES

- Meiotic nondisjunction in one parent
 - Trisomy 13 (47 XY, +13)
- Translocation of chromosome 13

- Trisomy 13 mosaicism due to mitotic nondisjunction
 - Some cells unchanged (46 XY), others (47 XY, +13)

RISK FACTORS

- Family history, advanced maternal age

COMPLICATIONS

- Intrauterine growth restriction
- Multi-organ congenital anomalies (e.g. **severe intellectual disability**, capillary hemangioma, cardiac septal defects, cryptorchidism bicornuate uterus, intrauterine growth retardation, cerebral hypoplasia)
- **High mortality**
 - Most fetuses die in utero/stillborn; neonates die shortly after birth (median survival is seven days)

SIGNS & SYMPTOMS

- Anophthalmia, **microphthalmia**, cyclopia, colobomas
- **Holoprosencephaly** (formation of single forebrain with single ventricle)
- **Microcephaly**, neural tube defects, deafness
- **Cleft palate/lip**, **cutis aplasia**, omphalocele, post-axial **polydactyly**, prominent heel (**rocker-bottom feet**), dextroposition, absent philtrum

DIAGNOSIS

DIAGNOSTIC IMAGING

Prenatal ultrasound

- Unchanged inhibin A
- Nuchal translucency (weeks 11–14)
 - Holoprosencephaly; ventriculomegaly; microcephaly; corpus callosum agenesis; cleft lip, palate; neural tube defects; omphalocele; single umbilical artery; radial aplasia; polydactyly

LAB RESULTS

- Prenatal diagnosis
 - **Amniocentesis/chorionic villus sampling (CVS)**: ↓ PAPP-A, serum β-hCG, uE3, AFP, quadruple screen
- Postnatal diagnosis
 - Fluorescence in situ hybridization (FISH), karyotyping

OTHER DIAGNOSTICS

- Postnatal
 - Clinical identification of dysmorphic features



Figure 29.3 An adolescent female with Patau syndrome.



Figure 29.4 An infant with a more severe case of Patau syndrome demonstrating cyclopia and a proboscis.

TREATMENT

SURGERY

- Intensive treatment
 - Surgical repair of cardiac defect, cleft lip/palate

OTHER INTERVENTIONS

- Prenatal genetic counseling
- Noninterventional paradigm
 - Palliative, supportive management

FIRST TRIMESTER SCREENING FOR TRISOMIES

	NUCHAL TRANSLUCENCY	PAPP-A	FREE β -hCG
TRISOMY 21	↑	↓	↑
TRISOMY 18	↑	↓	↓
TRISOMY 13	↑	↓	↓

SECOND TRIMESTER SCREENING FOR TRISOMIES

	uE3	AFP	hCG	INHIBIN A
TRISOMY 21	↓	↓	↓	↑
TRISOMY 18	↓	↓	↓	Normal
TRISOMY 13	↓	↓	↓	Normal